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EXAMINER

STRZELECKA, TERESA E

ART UNIT

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1637

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/821,689

**Applicant(s)**

WILLIAMS, JOHN G.K.

**Examiner**

TERESA E. STRZELECKA

**Art Unit**

1637

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 May 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-46 is/are pending in the application.
- 4a) Of the above claim(s) 4-17, 20, 21, 24, 25 and 27-46 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 18, 19, 22, 23 and 26 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

1. This office action is in response to an amendment filed May 16, 2008. Claims 1-46 were previously pending, with claims 4-17, 20, 21, 24, 25 and 27-46 withdrawn from consideration.
  2. Applicants amended claims 1 and 29. Claims 1-3, 18, 19, 22, 23 and 26 will be examined.
  3. Applicants' amendments did not overcome any of the previously presented rejections.
- Applicants' arguments are addressed in the "Response to Arguments" section below.

#### ***Response to Arguments***

4. Applicant's arguments filed May 15, 2008 have been fully considered but they are not persuasive.

A) Regarding the rejection of claims 1-3, 18, 19 and 26 under 35 U.S.C. 102(b) as anticipated by Yao et al., Applicants argue that the PCNA molecule of Yao et al. is not a part of the attachment complex comprising at least one anchor which irreversibly associates the target nucleic acid with the polymerase, since in order to accommodate the anchor, the polymerase itself must also be modified as an attachment complex.

However, Applicants argue limitations which are not in the claims. Applicants seem to argue that the attachment complex must be covalently bound to the polymerase: no such limitation is present in the claims, and there is no definition of the terms of "attachment complex" and "polymerase has an attachment complex". The only requirement of the claims is functional, i.e., that the attachment complex irreversibly associates target nucleic acid with the polymerase until the replication is complete, which is what the PCNA molecule does.

Applicants further argue that a skilled person would not understand the term "irreversible association" as interpreted by examiner. However, the only irreversibility required by the claims is during the replication process, which, again, is achieved by the PCNA molecule.

The rejection is maintained.

B) Regarding the rejection of claims 1-3, 18 and 26 under 35 U.S.C. 102(a) as anticipated by Motz et al., Applicants argue that the PCNA molecule of Motz et al. has the same properties as other PCNA molecules, and therefore recycling of PCNA is not an irreversible association as claimed.

Applicants argue parts of the reference which were not cited to support the rejection. Motz et al. teach using a modified Taq DNA polymerase which incorporates a binding site for the PCNA protein. Therefore, after addition of PCNA, which then binds to the Taq polymerase and stays bound during the replication process, the processivity of the polymerase is increased as a result, since the presence of PCNA prevents the target nucleic acid from diffusing away from the polymerase during replication, therefore irreversibly associating the polymerase with the target nucleic acid during the replication process, as required by the claims. The fact that PCNA is recycled outside of the replication process is irrelevant to the claimed subject matter.

The rejection is maintained.

C) Regarding the rejection of claims 19 and 22 over Motz et al. and Blanco et al., Applicants argue that Motz et al. does not suggest claim 1, therefore the rejection is improper. This argument was addressed above.

The rejection is maintained.

D) Regarding the rejection of claim 23 under 35 U.S.C. 103(a) over Williams and Motz et al. Applicants argue that since claim 1 is patentable, it cannot be obvious.

The patentability (or lack thereof) of claim 1 was addressed above.

The rejection is maintained.

***Claim Interpretation***

5. The term “attachment complex” has not been defined by Applicant, therefore it is considered as any molecule. Further, the term “polymerase has an attachment complex” is interpreted as “polymerase comprises an attachment complex” and the attachment complex may be covalently or non-covalently linked to the polymerase.
6. Applicant did not define the term “anchor”, therefore it is considered as any molecule.
7. Applicant did not define the term “modified amino acid”, therefore any modification, i.e., labeling, attachment of other amino acids, etc. is considered to anticipate this term.
8. Applicant did not define the term “irreversible association”, therefore, any association is considered as irreversible, provided the time scale or topological constraints.
9. Applicant defined the term “processivity index” on page 7, [0038], as the number of nucleotides sequenced divided by the number of nucleotides in the template.

***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-3, 18, 19 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Yao et al. (Genes to Cells, vol. 1, pp. 101-113, 1996; cited in the previous office action).

Regarding claim 1, Yao et al. teach a polymerase-nucleic acid complex, where the polymerase comprises a gp45 clamp or a PCNA clamp (=attachment complex), which irreversibly associates the polymerase with the nucleic acid during the replication phase to increase processivity (page 111, last paragraph; page 112, paragraphs 1, 2 and 4; Abstract; page 104, third-fifth

paragraphs; page 105, first paragraph; Fig. 3). Yao et al. teach modified amino acids in the PCNA and gp45 proteins (page 102, fifth paragraph).

Regarding claim 2, Yao et al. teach a complex with a primer (page 111, last paragraph; page 112, first paragraph; page 104, third paragraph).

Regarding claim 3, Yao et al. teach that gp45 and PCNA have three subunits (= anchors) (page 101, first paragraph; page 102, first paragraph).

Regarding claim 18, Yao et al. teach circular DNA (page 111, last paragraph; page 112, first paragraph; page 104, third paragraph).

Regarding claim 19, Yao et al. teach that the circular DNA molecules were nicked (page 111, fifth paragraph), therefore they were inherently amplified by strand displacement.

Regarding claim 26, Yao et al. teach increased processivity of the polymerases with their processivity clamps (Abstract), and since the processivity depends of on the reaction conditions and a specific template, it is inherent that the processivity of the polymerase with the clamp would be at least 0.5 with respect to the polymerase without the clamp.

12. Claims 1-3, 18 and 26 are rejected under 35 U.S.C. 102(a) as being anticipated by Motz et al. (J. Biol. Chem., vol. 277, pp. 16179-16188, May 2002; cited in the IDS and in the previous office action).

Regarding claims 1 and 26, Motz et al. teach a Taq polymerase-nucleic acid complex, where the polymerase comprises a PCNA-binding domain and PCNA assembled on the binding domain (=attachment complex), which irreversibly associates the polymerase with the nucleic acid with the nucleic acid during the replication phase to increase processivity (Abstract; page 16180, second paragraph; page 16181, third and last paragraphs; page 16183, second paragraph; page 16186, second and third paragraphs; Fig. 4). Motz et al. teach a Taq DNA polymerase with a PCNA

binding motif (=an anchor), which is modified at its N-terminus by the presence of a six amino acid linker and 42 amino acid polB C-terminal amino acids (Fig. 4A).

Regarding claim 2, Motz et al. teach primers for the target nucleic acid (page 16181; third paragraph).

Regarding claim 3, Motz et al. teach PCNA and the PCNA-binding domain, therefore they teach two anchors (page 16183, second paragraph).

Regarding claim 18, Motz et al. teach circular DNA (page 16181; third paragraph).

***Claim Rejections - 35 USC § 103***

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

14. Claims 19 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Motz et al. (J. Biol. Chem., vol. 277, pp. 16179-16188, May 2002; cited in the IDS and in the previous office action) and Blanco et al. (U.S. Patent No. 5,198,543 A; cited in the previous office action).

A) Motz et al. teach Taq DNA polymerase, but do not teach strand displacement synthesis or polymerases of claim 22.

B) Blanco et al. teach using phi29 DNA polymerase for strand displacement amplification and sequencing (col. 1, lines 9, 10; col. 2, lines 3-35; col. 4, lines 18-52; col. 8, lines 46-51 and 54-57).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the phi29 DNA polymerase of Blanco et al. as a polymerase of Motz et al. Blanco et al. specifically teach that phi29 polymerase can be used in place of a Taq polymerase (col.

8, lines 54-57). The motivation to do so, provided by Blanco et al., would have been that the polymerase did not require temperature cycling and produced long strands of DNA (col. 8, lines 46-51).

15. Claim 23 is rejected under 35 U.S.C. 103(a) as being unpatentable over Williams (U.S. Patent No. 6,255,083 B1; cited in the previous office action) and Motz et al. (J. Biol. Chem., vol. 277, pp. 16179-16188, May 2002; cited in the IDS and in the previous office action).

A) Regarding claim 23, Williams teaches sequencing of nucleic acids using DNA polymerases immobilized on solid supports and Klenow DNA polymerase (col. 2, lines 16-36; col. 14, lines 21-58) as well as Taq polymerase (col. 17, lines 43-58). Williams does not teach irreversible association of the polymerase with nucleic acid target.

B) Motz et al. teach a Taq polymerase-nucleic acid complex, where the polymerase comprises a PCNA-binding domain and PCNA assembled on the binding domain (=attachment complex), which irreversibly associates the polymerase with the nucleic acid to increase processivity (Abstract; page 16180, second paragraph; page 16181, third and last paragraphs; page 16183, second paragraph; page 16186, second and third paragraphs; Fig. 4).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used the modified Taq polymerase of Motz et al. in the nucleic acid sequencing method of Williams. The motivation to do so, provided by Motz et al., would have been that the modification increased the Taq polymerase processivity (page 16186, second paragraph; Fig. 4).

16. No claims are allowed.



***Conclusion***

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA E. STRZELECKA whose telephone number is (571)272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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August 13, 2008